REMARKS

Upon entry of this amendment, claims 1, and 71-79 will pending. Claims 78 and 79 have been added. Support for claim 78 and 79 may be found throughout the specification of application 08/870,608, as originally filed, for example at page 29, line 23 through page 37, line 9; page 16, line 22 through page 17, line 2; and page 17, lines 15-25. Thus the amendments do not introduce new matter. Claim 69 is hereby canceled without prejudice

Double Patenting

Claims 1, 9, 59, and 68-72 were provisionally rejected as allegedly "unpatentable over claims 1, 5, 8, 19-22, 54, 57, and 63 of copending Application No. 10/700697." Office Action at page 4. Claims 1, 9, 59, and 68-72 were also provisionally rejected as allegedly "unpatentable over claims 1, 7-9, 16, 18-22, 26-31, 73, and 76-85 of copending Application No. 10/701,264." Office Action at page 5. Claims 1, 9, 59, and 68-72 were also provisionally rejected as allegedly "unpatentable over claims 1, 5, 9, 11, 75, 78, and 93-97 of copending Application No. 10/701,316." Office Action at page 6. Applicants respectfully request that these provisional rejections based on obvious type double patenting be held in abeyance until claims are found otherwise allowable.

Claim Objections

The Examiner objected to claim 74, because it was identical to claim 69. Applicants apologize for this error. Claim 69 has been canceled, thus obviating the objection.

Rejection Under 35 U.S.C. § 102

Claims 1, 69, and 74-76 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Bevilacqua et al., Biochemistry, 1996 (Bevilacqua). See Office Action at page 4. Claim 1 recites a first chemically synthesized oligomeric compound that is "100% complementary to . . . a selected target mRNA." Since the modified sequence in Bevilacqua is not 100% complementary to a target mRNA, Bevliacqua does not anticipate claim 1.

The Examiner remarked that "Bevilacqua et al. disclose (see figure 5 and description on page 9988, first column) chimeric dsRNA duplexes that correspond to the 22 nucleotides of the

TAR gene." Office Action at page 8. As noted in the previous response, however, TAR is not an mRNA, but rather is an untranslated regulatory sequence of HIV RNA. In response, the Examiner asserted that "the instant specification defines the **targeted sequences** broadly as encompassing any nucleic acid capable of being targeted, therefore even though TAR is an untranslated sequence it nevertheless meets the definition of a target **mRNA**." Office Action at page 6 (emphasis added). The Examiner seems to contend that if the term "targeted sequence" is broad enough to reach TAR, then so too is the term "target mRNA" as recited in the pending claims. Applicants disagree. It is axiomatic that claims are defined by their terms.

During examination, claims are given their broadest reasonable meaning. See M.P.E.P. § 2111.01. According to the M.P.E.P, "[t]his means that the words of the claim must be given their plain meaning unless the plain meaning is inconsistent with the specification." Id. As noted by the Examiner, the specification broadly defines "target nucleic acid" to include "any nucleic acid capable of being targeted." Specification at page 15. That term, however, is not recited in the presently rejected claims. Rather, claim 1 recites "target mRNA." The plain meaning of "mRNA" is an RNA molecule transcribed from the DNA of a gene and from which a protein is translated. See, e.g., A.L. Lehninger, Biochemistry, second edition (1975), pages 320-322 (copy provided as Appendix A)(Lehninger). That definition is consistent with the use of the term mRNA in the present specification. See e.g., Specification at pages 15-16 (describing target mRNA as a sub-set of target nucleic acid); pages 36-38 (discussing certain mRNA targets). As noted in the previous response, the TAR sequence discussed in Bevilacqua is a regulatory sequence of HIV and thus cannot reasonably be considered an mRNA. For at least that reason Bevilacqua fails to anticipate the present claims.

Moreover, as noted previously, Bevilacqua does not even provide compounds that are 100% complementary to the TAR regulatory region of HIV. Bevilacqua does indeed disclose the TAR sequence. See Figure 1A. However, Bevilacqua describes that that sequence was twice altered prior to forming the duplex. First, it was altered to create dsTAR, an artificial construct in which, "three bulges are deleted and G-U wobble pairs converted to G-C base pairs." Id, at page 9986, first column. Then that dsTAR sequence was further altered for the experiments reported in Figure 5, cited by the Examiner as anticipatory. One need only compare the sequences provided in the legend of Figure 5 with the original TAR sequence provided in Figure 1A to note

the differences. Thus, as previously remarked, Bevilacqua fails even to disclose oligomeric compounds that are 100% complementary to TAR, which, as discussed above, also fails to meet the limitations of claim 1 because it is not an mRNA.

For at least those reasons Bevilacqua does not anticipate the present claims. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102 based on Bevilacqua.

Claims 1, 69, and 74-76 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Yu et al. (Yu). As noted in the previous response, Yu discusses compounds complementary to ribosomal RNA (rRNA). The present claims recite compounds complementary to target mRNA. A brief description these types of RNA may be found, for example, in Lehninger's Biochemistry textbook, referenced above and provided for the Examiner's convenience. Since rRNA differs from any reasonable definition of mRNA, Yu fails to anticipate the present claims to compounds complementary to a target mRNA.

Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 102.

Rejection Under 35 U.S.C. § 103

Claims 1, 69, and 71-77 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Yu in view of Stec et al., US 5,151,510 (Stec) and Summerton et al., US 5,142,047 (Summerton). Applicants respectfully traverse.

As described above, Yu discusses duplexes in which one strand is complementary to rRNA and not to mRNA as claimed. Nothing in Yu or in Stec or Summerton suggests applying the teaching of Yu to mRNA. For at least that reason, the claims are non-obvious in view of Yu, Stec, and Summerton.

Moreover, even if the teaching of Yu did reach mRNA, which it clearly does not, there is no reason why one would modify the duplexes in Yu to arrive at the claimed invention. According to the Supreme Court, a finding of obviousness requires identification of "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex*, 127 S.Ct. 1727 (2007). The Examiner asserts that "Yu et al. teach the at their duplex is useful in RNase H cleavage assays,

therefore one would incorporate modified nucleotides in order to test the modified duplexes for such activity." Office Action at page 9. Applicants disagree.

In naturally occurring rRNA, certain nucleosides are methylated. See e.g., Lehninger at page 322. Yu describes a method for determining whether a particular nucleoside of a natural rRNA is methylated. See Abstract at page 324. The method, as diagrammed at page 326, involves preparing a duplex comprising a natural rRNA (which may or may not comprise a methylated nucleoside at a particular position) and a chimeric oligonucleotide designed to support RNase H cleavage of the rRNA only at the position in question. Upon contact with RNase H, the rRNA of the duplex will be cleaved only if the nucleoside in question is not methylated, because RNase H will not cleave methylated RNA. Thus, one can determine the methlyation state of the nucleoside in question by determining whether cleavage occurs. One skilled in the art would have no reason to modify the native rRNA either to enhance or inhibit nuclease activity. Indeed, such modification would frustrate the very purpose of the assay described in Yu. The Examiner cited Stec and Summerton for modifications not found in Yu. Those references fail to provide any reason to modify a duplex and thus, fail to remedy the deficiencies of Yu.

Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103 based on Yu in view of Stec and Summerton.

Conclusion

Applicant believes that the foregoing constitutes a complete and full response to the official action of record. Accordingly, an early and favorable action is respectfully requested.

Respectfully submitted,

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